COMPLETE SET OF AMENDED CLAIMS IN CLEAN FORM

We claim:

1. (Amended) A method for determining if a test compound induces uracil misincorporation into DNA, the method comprising:

a) providing aliquots of the following cells:

i) wildtype cells;

ii) cells overexpressing dUTPase;

iii) cells overexpressing a uracil-DNA glycosylase; and

iv) cells expressing the uracil-DNA glycosylase inhibitor protein Ugi or cells possessing a compromised uracil-DNA glycosylase function;

b) exposing the cells to an agent that directly or indirectly inhibits thymidylate metabolism, in the presence or absence of the test compound;

c) measuring one or more features of the exposed cells, the features comprising:

i) cell growth or viability;

ii) cell cycle checkpoint arrest;

iii) presence of replication intermediates in the cells;

iv) amount of dUTP present in the cells; and

v) presence or amount of uracil in DNA of the cells; and

d) interpreting the measured features, wherein a profile in the four cell types which is indicative that the test compound induces uracil mis-incorporation into DNA comprises one or more features in each of the cell types comprising:

i) in the wildtype cells, cytotoxicity, cell cycle arrest at G1/S or early S phase, presence of replication intermediates, elevated dUTP pools or little or no detectable uracil in the DNA;

ii) in the dUTPase overexpressing cells, enhanced resistance to cytotoxicity, cell cycle arrest at mid S-phase, presence of replication intermediates, low dUTP pools, or little to no detectable uracil in DNA

iii) in the uracil-DNA glycosylase overexpressing cells, cytotoxicity or enhanced cytotoxicity, cell cycle arrest at G1/S or early S-phase, presence of replication intermediates, elevated dUTP pools, or little to no detectable uracil in DNA; and

iv) in the nonfunctional uracil-DNA glycosylase cells, enhanced resistance to cytotoxicity, cell cycle arrest at G2/M phase, reduced presence of replication intermediates, elevated dUTP pools, or stable uracil incorporation into DNA.

2. The method of claim 1, wherein the cells are of an organism selected from the group consisting of yeast, *D. melanogaster*, and *C. elegans*.

3. The method of claim 2, wherein the cells are yeast cells and the conversion of dUMP to TMP is inhibited by an antifolate.

4. The method of claim 3, wherein the antifolate is selected from the group consisting of aminopterin and sulfanilamide.

5. (Amended) The method of claim 1, wherein the cells overexpress a dUTPase from an organism selected from the group consisting of humans, animals, plants, fungi, algae, protozoa, bacteria and viruses.

6. (Amended) The method of claim 1, wherein the cells overexpress a uracil-DNA glycosylase from an organism selected from the group consisting of humans, animals, plants, fungi, algae, protozoa, bacteria and viruses.

7. (Amended) The method of claim 1, wherein the cells lacking a uracil-DNA glycosylase function are produced by producing in the cells an inhibitor of uracil-DNA glycosylase.

8. (Amended) The method of claim 1, wherein the inhibitor of uracil-DNA glycosylase is obtained from a virus.

9. (Amended) The method of claim 1, adapted for determining if the test compound inhibits dUTPase, the adaptation comprising, in step (d), observing in each of the four cell types one or more features comprising:

i) in the wildtype cells, cytotoxicity, cell cycle arrest at, G1/S or early S phase, presence of replication intermediates, elevated dUTP pools, or little or no detectable uracil in the DNA;

ii) in the dUTPase overexpressing cells, continued growth resistance to cytotoxicity, cell cycle arrest not present or, if present, occurring at mid S-phase, presence or absence of replication intermediates, low dUTP pools, or little to no detectable uracil in DNA;

iii) in the uracil-DNA glycosylase overexpressing cells, cytotoxicity or enhanced cytotoxicity, cell cycle arrest at G1/S or early S-phase, presence of replication intermediates, elevated dUTP pools, or little to no detectable uracil in DNA; and

iv) in the uracil-DNA glycosylase inhibitor (Ugi) expressing cells, enhanced resistance to cytotoxicity, cell cycle arrest at G2/M phase, reduced presence of replication intermediates, elevated dUTP pools, or stable uracil incorporation into DNA.

10. The method of claim 1, wherein two or more test compounds are added to the aliquots of cells.

11. (Amended) A kit comprising:

a) aliquots of the following cells:

i) wildtype cells;

ii) cells overexpressing dUTPase;

iii) cells overexpressing a uracil-DNA glycosylase; and

iv) cells lacking a uracil-DNA glycosylase function; and

b) instructions for using the cells in an assay to determine if a test compound induces uracil misincorporation into DNA.

12. (Amended) A method for determining the effectiveness in a patient of chemotherapy targeting conversion of dUMP to TMP, the method comprising:

a) obtaining from the patient a sample of cells which are the target of the chemotherapy;

b) measuring one or more features of the cells, the features comprising:

i) cell growth or viability;

ii) cell cycle checkpoint arrest;

iii) presence of replication intermediates in the cells;

viii) amount of dUTP present in the cells; and

ix) presence or amount of uracil in DNA of the cells; and

c) observing if one or more of the measured features is the same as or differs from features comprising: cytotoxicity, cell cycle arrest at G1/S or early S-phase, presence of replication intermediates, elevated dUTP pools or little or no detectable uracil in the DNA, wherein a lack of divergence from one or more of the features is indicative that the chemotherapy is effective, and a divergence from one or more of the features indicates a possibility that the chemotherapy is of reduced effectiveness or is ineffective.